Biology Of Peri Implant Tissues: A Review

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Abstract
Dental implants are known to humans for thousand years and have been used time and again for replacement of missing teeth. In modern day scenario, Implants have emerged as an convincing approach towards rehabilitation of mastication, speech and aesthetics in dentistry with thediscovery of Titanium based endosseous implants. The work of Branemark and the concept of osseointegration has bought an evolution in implant dentistry.The successful implant osseointegration depends on peripheral tissues.As placement of implants nowadays is a common practise, there is a need to interchange information regarding the biology of peri implant tissue to ensure a successful implant placement and maintainance.This review briefs the biological width concept, osseointegration and hard & soft tissue interfaces around an implant.
Keywords: Dental Implant; osseointegration; peri-implant tissue;

I.   Introduction

Since ancient Egyptian times, dated back to 2000 B.C. several researchers tried to replace the lost teeth by means of different implant materials such as ivory, seashells, bamboo and even metals. These materials were not able to provide a long term result as they could not integrate with the periodontium around them. The result, regardless of material or design, was unsatisfactory clinically and there was a soft tissue layer seen interposed between the implant and bone during the healing process. This in turn led to pain, mobility and eventually failure of those implants. In 1940, Formiggini and Zepponi introduced a post type endosseous implant having a spiral stainless steel design which allowed the bone to grow into the metal(1). In 1952, Per Ingvar Branemark, who is currently known as Father of Dental Implants coined the term osseointegration i.e. close integration with the bone. Branemark in his studies on bone healing and regeneration saw that titanium chamber placed into rabbit femur attracted bone to grow around it and it was extremely difficult to retrieve it from the bone. This phenomenon of osseointegration marked a new revolution in the field of implant dentistry(2). Today, implants have become a common choice for replacement of missing teeth. But still in the present time, we encounter certain implant failures after more than forty years of the first titanium based dental implant placed in a human volunteer in 1965 by Branemark. The major reason in our prespective is a lack of knowledge about the interactions of an implant with the host tissue. Thus, this article highlights the biology and anatomical changes in the periodontium around an implant to attain a better and precise approach towards successful implant placement and dental rehabilitation of the patient.

HARD TISSUE INTERFACE OF AN IMPLANT
Dental implants placed in the jaw bones cause trauma to the underlying bone as the process involves osteoectomy of the bone to account for space needed for implant placement.

BONE
Bone healing around implants involves a cascade of cellular and extracellular biological events that take place at the bone-implant interface until the implant surface appears finally covered with a newly formed bone. This cascade of injury due to implant placement and host response activation includes hematoma

formation and mesenchymal tissue development, woven bone formation through the intramembranous pathway, and lamellar bone formation on the spicules of woven bone.

Blood is the first biological component to come into contact with an endosseous implant. Blood cells including red cells, platelets, and inflammatory cells such as polymorphonuclear granulocytes and monocytes migrate into the tissue surrounding the implant. The blood cells entrapped at the implant interface are activated and release cytokines and other soluble, growth and differentiation factors (3). Blood clot formation is marked as the initial host response. Platelets undergo morphological and biochemical changes as a response to the foreign surface including adhesion, spreading, aggregation, and intracellular biochemical changes such as induction of phosphotyrosine, intracellular calcium increase, and hydrolysis of phospholipids. The formed fibrin matrix acts as a scaffold (osteoconduction) for the migration of osteogenic cells and eventual differentiation (osteoinduction) of these cells in the healing compartment. Osteogenic cells form osteoid tissue and new trabecular bone that eventually remodels into lamellar bone in direct contact with most of the implant surface (osseointegration)(4).

Osteoblasts and mesenchymal cells migrate and attach to the implant surface and creates a non-collagenous calcified afibrillar matrix layer rich in calcium, phosphorus, osteopontin and bone sialoprotein on the implant surface that regulates cell adhesion and binding of minerals(5). The newly formed network of bone trabeculae ensures the biological fixation of the implant and surrounds marrow spaces containing many mesenchymal cells and wide blood vessels. A thin layer of calcified and osteoid tissue is deposited by osteoblasts directly on the implant surface. Blood vessels and mesenchymal cells fill the spaces between calcified tissues(3). This is followed by deposition of woven bone and arrangement of trabeculae. Woven bone is progressively remodelled and substituted by lamellar bone. At three months post-implantation, a mixed bone texture of woven and lamellar matrix can be found around different types of titanium implants(6). As adaptation to stress and mechanical loading bone around implants undergo remodelling.

BONE REMODELLING

Major factors for the failure of peri-implant osteogenesis include the decreased number and/or activity of osteogenic cells, the increased osteoclastic activity, the imbalance between anabolic and catabolic local factors acting on bone formation and remodelling, the abnormal bone cell proliferation rate and response to systemic and local stimuli and mechanical stress, and the impaired vascularization of the peri-implant tissue (7).

Bone tissue damage and debris created by the osteotomy site preparation must be cleared up by osteoclasts for normal bone healing. These multinuclear cells, originating from the blood, can resorb bone at a pace of 50 to 100 μm per day (8). There is a coupling between bone apposition and bone resorption. Preosteoblasts, derived from primary mesenchymal cells, depend on a favorable oxidation-reduction (redox) potential of the environment. Thus a proper vascular supply and oxygen tension are needed. If oxygen tension is poor, the primary stem cells may differentiate into fibroblasts, form scar tissue, and lead to implant failure (non-integration). If bone is overheated or crushed during preparation, it will become necrotic and may lead to non-mineralized (soft tissue) scar formation or be sequestered. Critical temperature for implant site preparation is 47 degree Celsius for 1 min. and 40 degrees for 7 min.During the remodeling of theperi-implant bone, new osteons circle around the implant with their long axis parallel to the implant surface and perpendicularto the long axis of the implants. Osteoid tissue isproduced by osteoblasts suggesting that osteogenesis isunderway. The remodelled bone can extend up to 1 mmfrom the implant surface (8,9).

SOFT TISSUE INTERFACE OF AN IMPLANT

The soft tissue interface of the implant had been neglected in the initial years of implant dentistry. Thanks to the work by the researchers in the last two decades soft tissue considerations in the implant established as an important factor for aesthetics and long term stability of implants. The major difference in the periodontal anatomy of a tooth and implant is that the later lacks a periodontal ligament support. Due to this fact, the earlier works of Branemark did not include soft tissue implant interface. Implants in the aesthetic zone demanded a better stabilisation of soft tissues to provide a better outcome for the prosthesis. This led to the study of soft tissues around implants which includes gingival/mucosal sulcus, a long junctional epithelial attachment, and a zone of connective tissue above the supporting bone.

BIOLOGICAL WIDTH

Biological width i.e. the distance between the margin of peri-implant mucosa and underlying bone crest has emerged as a pivotal factor for implant placement. It has been hypothesised that a relationship of bone to overlying soft tissue exists around implants and changes in this relationship may be one of the reasons for the early crest bone loss. Many studies showed that biologic width around implants consists of sulcular and junctional epithelium and an underlying connective tissue zone. The biological width around a tooth and an implant presents some differences. While in the tooth the biological width is found supracrestal, in implants it is situated subcrestal when the platform is at the level of the crest. The width is usually greater around the implant

(3 mm against 2 mm in the tooth). The histological composition is also different, since in the peri-implant tissue there are more collagen fibers that flow parallel to the surface, acting as a scar tissue, with smaller adhesion, while in the tooth the supracrestalfibers flow perpendicularly and they are inserted in the radicular cement and the alveolar bone. The tissue is also less vascularised, due to that it only receives contributing blood of the terminal branches of the periosteum, while in the tooth there is also contribution of branches that come from the periodontal ligament. That could influence negatively in the answer of the periimplant tissue against a bacterial invasion (10).

EPITHELIUM

The portion of the peri-implant mucosa that is facing the implant (abutment) contains two distinct parts, a "coronal" portion that is lined by a thin barrier epithelium (similar to the junctional epithelium of the gingiva) and sulcular epithelium, and a more "apical" segment in which the connective tissue appears to be in direct contact with the implant surface. Junctional epithelium (JE) is a specialized epithelium located at the base of gingival sulcus that connect soft gingival tissue to implant. Junctional epithelium attachment is marked by a high rate of cell turnover and the rapid reattachment of this specialized epithelium to the surgical site after the injury caused by drills needed to prepare implant space. The cut edge of healthy gingival mucoperiosteum differentiates to produce junctional epithelial attachment. JE being porous in nature allows influx of substance from outer environment into host tissue and efflux of tissue fluid into the external environment. Ultrastructural examination of the long junctional epithelial attachment adjacent to dental implants has demonstrated that epithelial cells attach with a basal lamina and hemidesmosomes (11).The junctional epithelium which seals the periodontal tissue from the oral cavity, is surrounded on a basement membrane (BM) comprising two layers (internal and external basement laminae (IBL and EBL, respectively)), which are divided into electron-lucent and electron-dense laminae (the lamina lucida (LL) and lamina densa (LD), respectively), through which the epithelial cells of the JE attaches to tooth surface. On the enamel side, the LL connects to the JE cells, an interaction that is reinforced by hemidesmosomes, epithelial adhesion plaques that tack the plasma membrane of the epithelial cells to the adjacent LL. The LD is connected to the enamel. The BM forms an interface between the epithelial and connective tissue.In health, the dimension of the sulcular epithelium is about 0.5 mm, and the dimension of the epithelial attachment is about 2 mm,which is higher than that of the periodontal epithelial attachment. The apical edge of the epithelial attachment is about 1.5 to 2.0 mm above the bone margin. In healthy peri-implant tissues, progressive epithelial downgrowth does not occur.

CONNECTIVE TISSUE

This apical portion of the peri-implant mucosa is designated zone of connective tissue adhesion mainly comprised of collagen fibres and matrix elements (85%), comparatively few fibroblasts (3%), and vascular units (5%). The outer (oral) surface of the connective tissue is often covered by an orthokeratinized epithelium. In the connective tissue immediately lateral to the barrier and sulcular epithelium, a delicate plexus of vascular structures, similar to the dentogingival vascular plexus, is consistently present, while the connective tissue adhesion zone appears to harbour only limited amounts of vascular structures. With implants placed into masticatory mucosa, the main collagen fibre bundles are anchored in the crestal bone and extend in a marginal direction parallel to the surface of the metal device. It is assumed that circular fibres may also be present in this type of peri-implant mucosa (12).The role of connective tissue around both implant and tooth is not only for the protection from the external stimulation such as oral bacteria, but also for the supply of nutrients from the blood vessel.
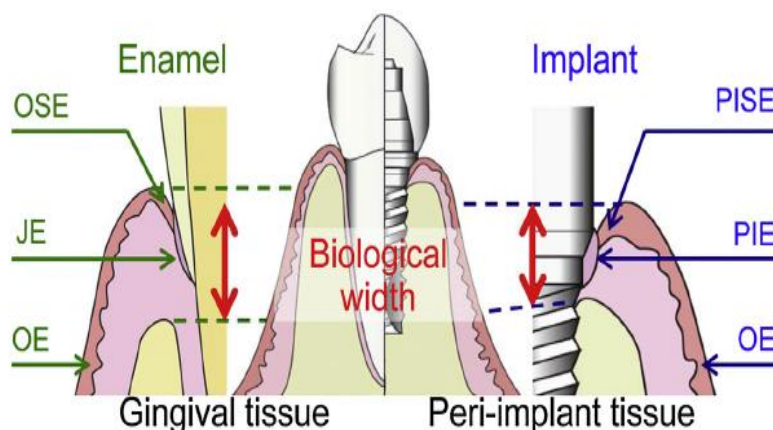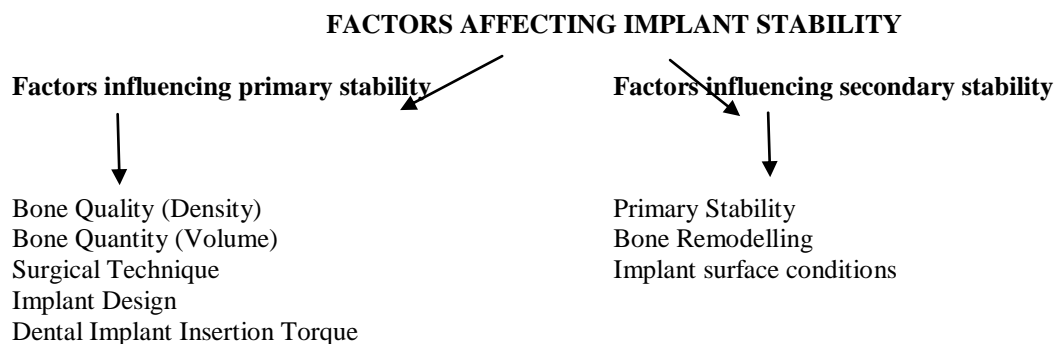

Fig. 1 – Landmarks of peri-implant and periodontal tissue. Diagram shows the key landmarks of the soft tissue attachment to natural tooth tissue (left panel) and their functional equivalents in the soft tissue attachment to an

implant surface (right panel). (JE: junctional epithelium, OSE: oral sulcular epithelium, OE: oral epithelium, PIE: peri-implant epithelium, PISE: peri-implant sulcular epithelium). (13)

FACTORS AFFECTING IMPLANT STABILITY

Factors influencing primary stability

Bone Quality (Density)
Bone Quantity (Volume)
Surgical Technique
Implant Design
Dental Implant Insertion Torque

Factors influencing secondary stability

Primary Stability
Bone Remodelling
Implant surface conditions

(**Table 1**- Factors Affecting Implant Stability)

Bone Quality and Quantity

Radiological bone quality evaluation is consideredan essential element during the pre-surgical implantplanning. Bone with high cortical density and smalltrabecular spaces was for a long time consideredthe ideal anatomy to ensure osseointegration. Bonequalityevaluations have therefore mainly focusedon trabecular bone density calculations and linearbone measurements. Nowadays, modificationin implant surface characteristics have immenselychanged the perception of optimal bone quality. Itwas reported that well-structured and vascularisedtrabecular bone is preferable to achieve a high implant success. The later implies that increasedtrabecular bone density is no longer a key factor forimplant success, making the need to measure multi-slicecomputed tomography (MSCT) based on Hounsfieldunits to express bone density (14).

Classification of Bone Density by Lekhotm and Zarb (1985)

Quality I bone: Compromised homogeneous compact bone

Quality II Bone: Thick layer of compact bone surrounding a core of dense trabecular bone.

Quality III Bone: Thin layer of cortical bone surrounding dense trabecular bone of favourable length.

Quality IV Bone: Thin layer of cortical bone surrounding a core of low-density trabecular bone.

Fig. 2- Classification of Bone Density

Implant Surface Characteristics&Implant Design:

Response of the tissues to the implant is largely controlled by the nature and texture of the surface of the implant. Compared to smooth surfaces, textured implants surfaces exhibit more surface area for integrating with bone via osseointegration process. Textured surface also allows ingrowth of the tissues. Endosseous dental implants are available commercially with many different surface configurations (15).Macro-irregularities in an implant include macroscopic threads, fenestrations, pores, grooves, steps, threads, or other surface irregularities that are visible. The idea is to create mechanical interlocking between implant and bone at the macro level. Micro-irregularities in an implant involves microscopic surface changes which are created to enhance the load transmitting capabilities of the interface and these can be created byinorganicmineral coatings, plasma spraying, biocoating with growthfactors, fluoride, and particulates or cements containing calcium phosphates, sulfates, carbonates or hydroxyapatite (16).
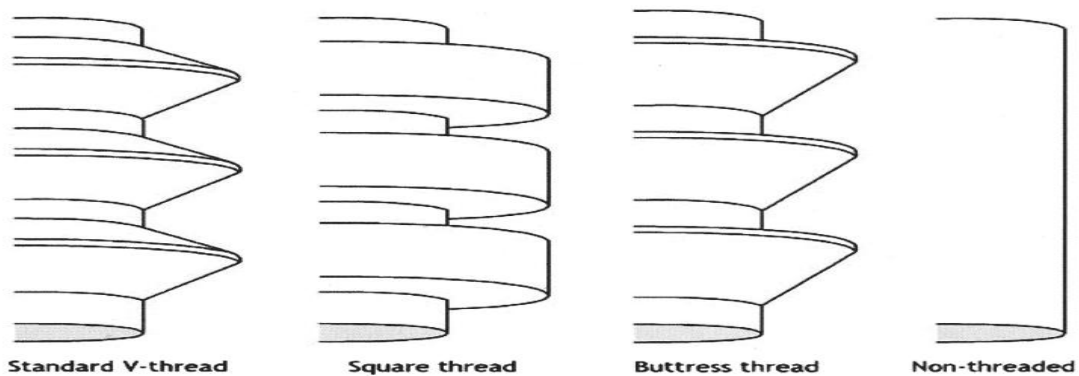
Fig: 3- Standard thread shapes in dental implant design. V-thread (Nobel Biocare, Paragon, 3i, Calcitek, ITI), square thread (Biohorizons), buttress thread (Steri-Oss), and cylindrical (nonthreaded). (17)

Thread patternsin dental implants currentlyrange from micro-threads near the neck of the implant (AstraTech, Lexington, MA) to broad macro-threads on the mid-body (Biohorizons,Birmingham,AL; Steri-Oss,NobelBiocare) and a variety of altered pitch threadsto induce self-tapping and bone compression (Implant Innovations, Palm Beach Gardens, FL; NobelBiocare). Thus a plethora of modifications have been employed by implant companies to accentuate the effect of threads. Although clinical evidence is unclear on the effects of implant thread shape on initial implant stability, it may be deduced that thread design may be influential in poor quality bone, and not be as significant in good quality bone. Implant neck (crest module), the highest bone stresses have been reported to be concentrated in the cortical bone in the region of the implant neck as demonstrated in Finite Element Analysis(FEA) of loaded implants with or without superstructure. This is consistent with findings from experiments and clinical studies that demonstrated that bone loss begins around the implant neck. It has been suggested that the implant neck should be smooth/ polished, supporting the belief that the crest module should not be designed for load bearing. However, significant loss of crestal bone has been reported for implants with 3 mm long smooth polished necks (18).

Dental Implant Insertion Torque:
Micromovement or motion between freshly placed implantandbone can jeopardise osseointegration. Therefore primary stability immediately postimplant placement and in the early healing phase is necessary till the time secondarystability is gained by bone remodelling and osseointegration.There is asharp reduction in interfacial strain due to mechanical stress relaxation in the bone. Insertion torque canprovide assessment of bone quality as a function of density and hardness, eithersubjectively in experienced hands or quantitatively by electronic drill devices whichmeasure the torque required to insert implant in the bone. With the use of compression techniques toachieve better stability, insertion torque could be improved in poor quality bone. Although, inducingover-compression could jeopardise the healing process. Under high stress, angiogenesisgets altered and it impairs new blood vessel formation. This leads to hypoxia in peri-implanttissues which inhibit bone formation and adversely affects stability.The tubulenetwork of bone is filled with interstitial fluid supplying the bone cells. It is able totransmit external stresses to bone cells through "Mechano-transduction". Mechanicalenergy from external stresses gets converted into bioelectric and biochemical signals thatmodulate bone cell metabolism. When this mechanical energy is too high, osteocytes areinduced to death, followed by emergence of osteoclasts and bone destruction ensues.This could affect the process of osseointegration.Neugebauer and associates considered insertion torqueabove 50 Ncm to be higher and should not be exceeded, whereas a torque of 35 Ncm wasconsidered optimum for immediate loading protocol. (19)

Criteria for Implant Success (Fig. 4,5,6)

Albrektsson et al. (1986) developed the following criteria that have become the standard by which implant success is determined (20):
1. That in an individual, unattached implant is immobile when tested clinically.
2. That a radiograph does not demonstrate any evidence of peri-implant radiolucency.
3. That vertical bone loss is less than 0.2 mm annually following the first year of service.
4. That individual implant performance is characterized by an absence of persistent and/or irreversible signs and symptoms such as pam, infection, neuropathies, paresthesias, or violation of the mandibular canal.
5. That, in the context of the above, a successful rate of 85% at the end of a 5-year observation period and 80% at the end of a 10-year period is a minimum criterion for success.

Fig. 4

This was modified by **Roos et al. (1997)** to include different grades of success for implants(21). The new classification is as follows:

Grade 1:
1. Absence of mobility is checked by individual testing of the unattached implant, using a light tightening force of an abutment screwdriver without simultaneous counteracting of the force via an abutment clamp. Any mobility or sensation/pain from the anchorage unit is regarded as a sign of lost osseointegration.
2. Radiographic evaluation of each implant reveals not more than 1.0 mm of marginal bone loss during the first year of loading, followed by not more than 0.2 mm resorption per year, as well as absence of periimplant pathosis, such as a peri-implant radiolucency.
3. Severe soft tissue infections, persistent pain, paresthesia, discomfort,etc , are absent.

Grade 2:
1. Radiographic evaluation of each implant reveals not more than 1.0 mm of marginal bone loss during the first year of loading, followed by not more than 0.2 mm resorption per year, as well as absence of periimplant pathosis, such as a peri-implant radiolucency.
2. Severe soft tissue infections, persistent pain, paresthesia, discomfort, etc, are absent.

Grade 3:
1. Radiographic evaluation of each implant reveals not more than 0.2 mm of marginal bone resorption during the last year, but previously more than 1.0 mm of bone loss has taken place. Peri-implant pathosis, such as a peri-implant radiolucency is absent.
2. Severe soft tissue infections, persistent pain, paresthesia, discomfort, etc, are absent.

Fig. 5

Buser et al. (1990) proposed the following criteria for implant success (22):
1. Absence of persistent subjective complaints, such as pain, foreign body sensation and/or dysaesthesia.
2. Absence of a recurrent peri-implant infection with suppuration
3. Absence of mobility
4. Absence of a continuous radiolucency around the implant
5. Possibility for restoration.

Fig. 6

MICROBIOLOGY AROUND IMPLANTS

Longitudinal studies have shown that successful implants are colonized by a predominantly Gram-positive, facultative flora, which is established shortly after implantation. In patients with bone loss and pocket formation around implants, Gram-negative anaerobic bacteria, particularly fusobacteria, spirochetes, and black-pigmenting organisms such as *Prevotella intermedia* were often present in high proportions. Antimicrobial treatment with agents specifically active against anaerobes could halt progression of peri-implant infections in such cases. Although there may be non-microbial primary causes for implant failure, certain studies show that Gram-negative anaerobes may play a role in periimplant infections, and that their elimination leads to improvement of the clinical condition (23).

II. Conclusion

This review takes a logicalprespective in convergence of information on the biological changes which occurs around an implant. The purpose of this article is to bridge the gap in our understanding about the hard and soft tissue reaction followed by implant placement which are quite different from the periodontium around a natural tooth.

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